REMARKS

Claims 19-35 are pending. Applicants have amended claims 19, 20, 26, 27, and 32-35, to correct punctuation and grammar; claims 27 and 33 have been amended to insert the generic name for DESFERAL; claims 26 and 33 have been amended to insert the correct the name for EDTA. These amendments are made to better clarify the scope of the present invention and not intended to narrow or limit the scope of the present invention. Claim 28 has been canceled without prejudice. The specification has been amended at pages 3 and 4 to insert the generic name for DESFERAL and to insert the correct the name for EDTA. No new matter has been added. Applicants respectfully request entry of the present amendment. Accordingly, claims 19-27 and 29-35 will be pending.

Objection to the Specification

The specification has been objected to for the use of the trademark Desferal, which should be capitalized and accompanied by its generic name.

In response, Applicants have amended the specification at pages 3 and 4 to recite "deferoxamine mesylate (DESFERAL)". Deferoxamine mesylate is the generic name for DESFERAL (*See*, PDR® Electronic Library™, 2003, page 1). Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the objection to the specification.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claims 27-28 and 33-35 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the recitation of "desferal", which is a trademark. Claim 28 has been rejected as being a duplicate of claim 27 since deferoxamine is the generic name for Desferal.

In response, applicants have amended claims 27 and 3 to recite "deferoxamine mesylate", the generic name for DESFERAL and to delete the trademark. Claim 28 has been canceled without prejudice. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 27 and 33-35.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 19-35 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Gierskcky et al. U.S. Patent No. 6,034,267 ("Gierskcky").

The Examiner states that Gierskcky teaches pharmaceutical compositions for treating or diagnosing a condition comprising an ester of Aminolevulanic acid (AIA) (sic). The Examiner states that Gierskcky teaches concentrations of the compounds of

about 1 to 50%, the use of chelating agents such as deferroxamine (sic), and methods of preparing and using ALA hexyl ester. The Examiner acknowledges that Gierskcky "fails to specifically use concentrations of ALA-esters in amounts of less than 1% and further specify the instant ranges of pH."

The Examiner asserts that "merely selecting proportions and ranges is not patentable absent a showing of criticality" (citations omitted), and that accordingly, in the absence of such a showing, it would have been *prima facie* obvious to optimize the concentration of Gierskcky's ALA-esters and their respective pH ranges because the ordinary artisan would have a reasonable expectation of success in achieving the desirable clinical outcome by modifying such values.

Applicants respectfully traverse the rejection and maintain that the pending claims are not *prima facie* obvious over Gierskcky.

In order to establish a *prima facie* case of obviousness, three criteria must be met: First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references (or references when combined) must teach all the claim limitations. (See, MPEP 2143) The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Initially, applicants note that Gierskcky is a U.S. national stage application under 35 U.S.C. §371 of PCT/GB96/00553, filed March 8, 1996, which published as WO96/28412 (hereinafter the "'412"). The '412 publication was previously cited against the subject application under 35 U.S.C. §102(b) and under 35 U.S.C. §103(a) in view of Chang et al. J. Photochem & Photobiol. 1997; 28 (2-3): 114-22; these rejections have been obviated by applicants March 10, 2003 amendment, which was entered upon the filing of a continued prosecution application on May 5, 2003. Since the Gierskcky disclosure is the same as the '412 publication and since the '412 publication does not render the present claims obvious for the reasons set forth in Applicants' aforementioned amendment, neither does Gierskcky.

Further, applicants note that no suggestion or motivation is provided by Gierskcky to modify the reference to arrive at the claimed invention. Moreover, as discussed below, no such suggestion or motivation is provided by the knowledge generally available to one of ordinary skill in the art to arrive at the claimed concentrations of ALA-esters below 1%. Neither does Gierskcky teach all the claim limitations, *i.e.*, ALA-ester doses lower than 1%.

Applicants submit that the claimed concentrations of ALA-esters provide unexpected results of producing higher amounts of protoporphyrin IX (PpIX) than 5-aminolevulinic acid (ALA) at much lower concentrations than ALA.

This conclusion is supported by the Declaration of Georges Wagnieres, Ph.D. under 37 C.F.R. §1.132, submitted herewith. Dr. Wagnieres is one of the co-inventors of the subject application. In the Declaration, Dr. Wagnieres describes the results of *in vitro* studies (paragraphs 10-12) and *in vivo* studies (paragraph 13). Comparative studies of administration of low doses of ALA-esters and high doses ALA were conducted, since high doses of ALA were used in photodynamic therapy at the time of the subject invention. Dr. Wagnieres also points out in paragraph 15 that at the time of the priority date of the subject application, in April 1998, the concentrations of ALA-esters studied were about two orders of magnitude higher than the concentrations of the present invention. Accordingly, one of skill in the art would have had no motivation to use the low doses of ALA-esters, and further, would have had no reasonable expectation of success in arriving at the claimed concentrations of the ALA-esters to achieve desired clinical results at that time of the invention. Therefore, neither Gierskcky nor the knowledge generally available to one of ordinary skill in the art at the time of the invention teach or suggest the claimed invention and the reasonable expectation of success thereof.

Since Gierskcky has not met the three criteria to establish a *prima facie* case of obviousness, the cited reference cannot render obvious the presently pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of presently pending claims 19-27 and 29-35 under 35 U.S.C. § 103.

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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